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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATT	ORNEY DOCKET NO.
09/4/2.5	68 12/27	7 <b>99</b> HAHRAMIAN	M	2281/102
002111		1.164.1.0.7.1.0.00	EXAMINER	
U02101 HM12/1009			PARAS JEJP	
125 SHMM	ER STREET		ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks** 

## Application No. Applicant(s) 09/472,558 BAHRAMIAN ET AL. **Advisory Action** Examiner Art Unit Peter Paras, Jr. 1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 10 September 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Thereifinal recondit	fore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a ejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in ion for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued ination (RCE) in compliance with 37 CFR 1.114.
	PERIOD FOR REPLY [check either a) or b)]
a) [ b) [	The period for reply expiresmonths from the mailing date of the final rejection.  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).
have be 37 CFR (b) abov	tensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee en filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in e, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any patent term adjustment. See 37 CFR 1.704(b).
	A Notice of Appeal was filed on <u>13 September 2001</u> . Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2.🛛	The proposed amendment(s) will not be entered because:
(a)	they raise new issues that would require further consideration and/or search (see NOTE below);
(b)	they raise the issue of new matter (see Note below);
(c)	they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d)	they present additional claims without canceling a corresponding number of finally rejected claims.
	NOTE: See Continuation Sheet.
3.	Applicant's reply has overcome the following rejection(s):
4.	Newly proposed or amended claim(s) would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5.🛛	The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
_	The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7.🛛	For purposes of Appeal, the proposed amendment(s) a)⊠ will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
	The status of the claim(s) is (or will be) as follows:
	Claim(s) allowed:
	Claim(s) objected to:
	Claim(s) rejected: <u>1-27, 50, and 52</u> .
	Claim(s) withdrawn from consideration:
8.	The proposed drawing correction filed on is a) ☐ approved or b) ☐ disapproved by the Examiner.
9.	Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s).
10.	Other:  Other:

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Continuation of 2. NOTE: further consideration and a new search would be required for the following claim limitations as recited in claim 11, step b: under conditions devoid of a selection for integration of the nucleic acid into a chromosomal site, so that expression of the endogenous gene in the population as a whole is inhibited even though such gene's sequence is not therein disrupted. Furthermore, the specification has not provided relevant teachings, guidance, or working examples that correlate to the muting of nucleotide sequences other than the nucleotide sequence encoding pro-a1(I) collagen in cultured rat fibroblasts. With only one working example directed to muting single nucleotide sequence it is unpredictable if other nucleotide sequences may be muted by the same method. The specification has not provided any guidance to that end. The prior enablement rejection was directed to the production of knockout mice, wherein known nucleotide sequences can be used to knockout a particular nucleotide sequence in a mouse as the originally filed claims clearly read on such technology. The newly proposed claim limitations would eliminate enablement concerns over knockout technology but raise new issues of enablement over muting of nucleotide sequences other than the nucleotide sequence encoding pro-a1(I) collagen as recited above.

Continuation of 5, does NOT place the application in condition for allowance because: the term "population" is indefinite because it is not clear which cell type are encompassed by the term population.